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AF/1615

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123

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Application of:	) Novel Formulations Comprising Lipid-Regulating Agents
Lipari et al.	)
	) Group Art Unit: 1615
Serial No. 09/216,242	)
	) Examiner: Gollamudi S. Kishore
Filed: December 18, 1998	)

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TRANSMITTAL LETTER

Commissioner for Patents
Alexandria, Virginia 22313-1450

Sir:

In response to the Examiner's Answer dated December 3, 2003, Applicants submit herewith three (3) copies of the Reply Brief as required.

Respectfully submitted,

WOOD, PHILLIPS, KATZ, CLARK & MORTIMER

Martin L. Katz, Reg. No. 25,011

Date: February 3, 2004

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REPLY BRIEF

Commissioner for Patents
Alexandria, Virginia 22313-1450

Sir:

In response to the Examiner's Answer dated December 3, 2003 issued in the present application, this is the Appellants' Reply Brief.

Reply to Grounds of Rejection

In rejecting claims 1, 3-5, 12, and 14-17 under 35 U.S.C. 103(a) as being unpatentable over Lacy (U.S. Patent No. 5,645,856), further in view of Babayan (U.S. Patent No. 4,952,606), Bistraian (U.S. Patent No. 4,871,768), and Hyltander (NCP, 1995), individually or in combination the Examiner stated, "Appellant's arguments have been fully considered, but are not found to be persuasive. Appellant's arguments center around 'structured lipid.' These arguments have been extensively addressed before in Paper No. 25. In essence, according to applicant, capric and/or caprylic triglycerides taught by Lacy are not structured lipids. These arguments are not found to be persuasive. Applicant's statement on page 3 of the specification is as follows: 'Representative structured lipids include, but not limited to, caprylic/capric/lauric triglycerides, e.g., Captex 350™ (Abitec) and caprylic/capric/linoleic triglycerides, e.g., Captex 810 series (Abitec) and Miglyol 818 (Creanova), and in general, include those lipids containing saturated medium and long chain fatty acids esterified to the same glycerol molecule.'"

Lacy, on col. 9, lines 20-28, does teach several triglycerides under the trade names Miglyol and Captex; however, the Miglyol and Captex triglyceride oils specified are capric and/or caprylic triglyceride oils (column 9 lines 23-24). These disclosed oils are medium chain triglycerides, not structured lipids, as disclosed or claimed in the present invention. Structured lipids contain BOTH saturated medium and long chain fatty acids esterified to the SAME glycerol molecule (NCP, Vol. 10, No. 3, pp.89-90, June 1995 and Hyltander). Lacy discloses examples of several useful Miglyol (e.g., 810 and 812) and Captex (e.g., 300, 355, and 8000) capric and/or caprylic triglyceride oils. The present

invention discloses several representative structured lipids, e.g., Miglyol 818, Captex 810 series, and Captex 350. Even though the same trade names are used (i.e., Captex or Miglyol), it is the number designation which follows the trade name that completely differentiate these materials.

Attached hereto as Appendix A is a product catalog from Abitec that clearly describes the chemical and biological differences between medium chain lipids and structured lipids (refer to page 8 for the technical classification of Captex 300, 355, and 8000 vs. Captex 350 and 810D and to page 13 for biological differences).

The Examiner also stated, "It would appear that in the art that the term 'structured lipids' is given different interpretation and therefore, the interpretation given the references of Chavkin and Kikuchi is pertinent since instant claim 1 does not recite the specific lipids which applicant considers as structured lipids."

Applicants' interpretation of structured lipids agrees with the published literature (i.e., NCP, Vol. 10, No. 3, pp.89-90, June 1995, Hyltander, and Abitec's Captex product catalog).

Chavkin uses the term "structured" in the sense of being a "manufactured" lipid material (column 1, line 61) and specifically that material derived by the re-esterification of a high purity fatty acid (specifically, capric or decanoic acid, a medium chain fatty acid) and glycerin to yield a medium chain triglyceride (column 1 lines 60-63 and column 2 lines 1-3). This material is NOT a lipid containing both medium- and long-chain fatty acids esterified to the same glycerol molecule (i.e., a structured lipid as defined in the present invention or as defined in the published literature). The present invention teaches

"structured" lipids; capric triglyceride (as taught by Chavkin) is a "manufactured" tricaprin designated as a medium chain triglyceride.

Kikuchi teaches medium chain triglycerides as structured lipids (column 2, lines 24-34). However, Kikuchi uses the terminology "structured" as being those lipids that are "synthesized" (similar to Chavkin), NOT as a lipid containing both medium- and long-chain fatty acids esterified to the same glycerol molecule (i.e., a structured lipid as defined in the present invention or as defined in the published literature). Kikuchi describes only medium chain triglycerides (MCTs).

The Examiner further stated, "Appellant argues that instant claims now recite 'consisting of' and therefore, excludes the surfactants. Applicant further argues based on teachings of Lacy on col. 3, lines 41-42 that instant invention does not exhibit or demonstrate the property of 'not substantially inhibiting the lipolysis of the oil.' These arguments are not found to be persuasive since as pointed out before, instant specification clearly indicates that surfactants can be added (see example 1 in instant specification); in fact, it would appear from the comparison between figure 1 and figure 2, the plasma concentrations of fenofibrate are higher in the presence of surfactant than without it. Applicant has not shown any unexpected results by not including the surfactant as suggested by Lacy as argued."

The present invention claims a composition consisting of a fibrate dissolved in at least one structured lipid and discloses in Example 2 and Figure 2, compositions containing fenofibrate (a fibrate) simply dissolved in an example structured lipid (i.e., Miglyol 818); a surfactant component is not present. The data presented in Figure 2,

where the composition of Example 2 is dosed orally to dogs, demonstrates an equivalent oral bioavailability of fenofibrate when compared to the commercially available reference product, Lipanthyl 67M.

Lipanthyl 67M is a comicronized formulation of fenofibrate with a solid surfactant. The comicronized formulation is described in United States Patent No. 4,895,726 (disclosed in the Background of the Invention of the present application), and is manufactured via a complicated, expensive, and time consuming process. The process involves the steps of (i) intimately mixing and then comicronizing the fenofibrate and a solid surfactant; (ii) adding lactose and starch to the mixture obtained; (iii) converting the mixture to granules in the presence of water; (iv) drying the granules until they contain no more than 1% water; (v) grading the granules; (vi) adding polyvinylpyrrolidone and magnesium stearate; and (vii) filling into gelatin capsules. This comicronized formulation is a dramatic improvement over previously marketed fenofibrate formulations, such as Lipanthyl 300 (refer to U.S. Patent No. 4,895,726).

The present invention, consisting of a fibrate dissolved in at least one structured lipid, eliminates the need for such a complicated formulation and formulation process and results in a composition that demonstrates equivalent oral bioavailability to an enhanced reference product. The compositions of the present invention require only one excipient, i.e., at least one structured lipid, and only two formulation process steps, i.e., dissolving a fibrate in at least one structured lipid, followed by direct encapsulation. Surfactants may have a positive effect on bioavailability, but are not an essential requirement, as they are not necessary to produce a composition demonstrating an enhanced oral bioavailability that is

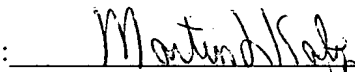
equivalent to the enhancement demonstrated by a comicronized formulation.

Compositions consisting of a fibrate dissolved in at least one structured lipid, and demonstrating oral bioequivalence to an enhanced reference product as presently claimed are unobvious in view of Lacy, Babayan, Bistrian, and Hyltander, individually or in combination.

Favorable consideration and reversal of the rejection of claims 1, 3-5, 12 and 14-17 for the above reasons and those set forth in APPELLANTS' BRIEF is respectfully requested.

Respectfully Submitted,

WOOD, PHILLIPS, KATZ, CLARK & MORTIMER

By: 

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Rebecca J. Willis

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